arthritis symptoms treating effective amount of erythropoietin over a treatment period, wherein said treatment period is at least 6 weeks, wherein said symptom is at least one symptom selected from the group consisting of morning stiffness, pain, loss of grip strength, painful joints, and swollen joints.

31. The method of claim 20, wherein the period is at least 6 weeks.

REMARKS

The amendments to the claims are supported by the specification at page 3, second paragraph, and Tables II-V. The amendment to Table V in page 13 is to correct a typographical error because the unit "mmH" means "millimeter height" which reflects the height of the erythrocytes in a capillary in which sedimentation of the erythrocytes was measured.

The amendments are made to more particularly point out and specifically claim the subject matter of what applicants regard as the preferred embodiments of the present invention.

Claims 14-26 and 30-31 are pending.

Claim Rejections -- 35 U.S.C. §112, Second Paragraph

A. Claims 18, 19, 23 and 24 were rejected as vague as to whether the scope of "symptoms associated with rheumatoid arthritis" refers to only the symptoms of

patients having arthritis or to the symptoms of patients of any diseases who happen to have the same symptom, e.g. pain, swelling or inflammation.

Applicant respectfully disagrees that the phrase "symptoms associated with rheumatoid arthritis" is vague. Applicant notes that "symptoms associated with rheumatoid arthritis" refers to only the symptoms of patients having rheumatoid arthritis, e.g. pain or joint swelling in patients having rheumatoid arthritis because the language "associated with rheumatoid arthritis" excludes symptoms not associated with rheumatoid arthritis, e.g. pain in patients not having rheumatoid arthritis.

The Examiner also wanted to know whether anemia in rheumatoid arthritis patients is included within the phrase "symptoms associated with rheumatoid arthritis". Applicant notes that anemia is excluded from "symptoms associated with rheumatoid arthritis".

B. Claims 20, 25 and 26 were similarly rejected as vague because the Examiner was not certain whether "a disease activity of rheumatoid arthritis" is limited to disease activities found in rheumatoid arthritis or to disease activities found in other diseases as well as in rheumatoid arthritis, e.g. anemia. Applicant notes that "a disease activity of rheumatoid arthritis" only refers to disease activities found in rheumatoid arthritis and claims 20, 25 and 26 are not drawn to methods of ameliorating a disease activity found in other diseases.

With the above explanations, withdrawal of the indefiniteness rejections is requested.

Claim Rejections -- 35 U.S.C. §112, First Paragraph

A. Claims 18, 19, 23 and 24 (methods for treating symptoms of rheumatoid arthritis) and claims 20, 25 and 26 (methods for ameliorating disease activities of rheumatoid arthritis) were rejected as not enabled for the full scope of the claims. The Office Action states that the nonenablement rejection would be withdrawn if applicant would limit claims 18, 19, 23 and 24 to only symptoms associated with rheumatoid arthritis and limit claims 20, 25 and 26 to disease activities found only in rheumatoid arthritis. As explained above, applicant does limit the meanings of

(a) "symptoms associated with rheumatoid arthritis" in claims 18, 19, 23 and 24 to only symptoms associated with rheumatoid arthritis; and

(b) "a disease activity of rheumatoid arthritis" in claims 20, 25 and 26 to disease activities found only in rheumatoid arthritis.

Withdrawal of the nonenablement rejection is requested.

B. Claims 14-17, 21 and 22 were rejected as not enabled because the Office Action asserts that the inventors fail to provide evidence that a reasonable

number of chronic inflammatory diseases are treatable with EPO. Applicant respectfully traverses the rejection.

The Office Action alleges that claims 14-17, 21 and 22 were not enabled because the specification does not have any evidence that EPO treats chronic inflammatory diseases other than rheumatoid arthritis. Applicant respectfully disagrees. Applicant notes that the enablement of claims is not necessarily limited to the scope of working examples under U.S. case law. See In re Borkowski, 164 USPQ 642, 645 (CCPA 1970); In re Angstadt, 190 USPQ 214, 218 (CCPA 1976). The Office Action repeats the former argument that one skilled in the art would not have reasonably predicted that EPO would be effective in treating chronic inflammatory diseases in general. However, the Office Action has failed to respond to the arguments presented in the Preliminary Amendment, page 6, second paragraph. Applicant incorporates by reference the arguments presented in the Preliminary Amendment. Applicant respectfully requests that the Patent Office explain why the method of treating chronic inflammation is not enabled when the specification already discloses that EPO induces a T_{h2} cytokine secretion proile and EPO counteracts the activity of tumor necrosis factor-alpha. Applicant specifically reiterates the argument as follows.

> "[T]he methods of claims 14-17, 22 and 23 are for treating chronic inflammation. The Final Office Action already admits that EPO affects the

cytokine levels. Pages 4 and 5 of the specification disclose that EPO induces a T_{h2} cytokine secretion profile. It is well known that cytokines play an important role in mediating the chronic inflammatory response. Page 5 of the specification discloses that EPO counteracts the activity of tumor necrosis factor-alpha, which is an important pro-inflammatory cytokines and EPO reduces the production of neutrophils, which are important in inflammation. Working examples also demonstrate that EPO is effective in treating chronic inflammatory symptoms of rheumatoid arthritis. Therefore, there is sufficient teachings in the specification that the claimed methods are effective in treating chronic inflammation, especially chronic inflammatory symptoms in immune diseases or auto-immune diseases, and to practice the claimed methods would not involve an unreasonable amount of experimentation based on the disclosure and what one skilled in the art already knows. Withdrawal of the nonenablement rejection is respectfully requested."

Applicant requests the Patent Office explain why, with a disclosure that EPO affects cytokines, that the methods of treating chronic inflammation are not enabled. Withdrawal of the nonenablement rejection is requested.

Claim Rejections -- 35 U.S.C. §103

Claims 14-26 were rejected as obvious over GB 2 171 304 (GB '304). Applicant respectfully traverses the rejection.

A. The methods of treating chronic inflammation of claims 14-17, 21 and 22 were rejected as obvious because the Office Action asserts that GB '304 teaches the treatment of anemia in patients having rheumatoid arthritis, i.e. an anemia of chronic disease, by administering EPO and because the Patent Office considered the anemia of chronic disease as a chronic inflammatory disease. Applicant respectfully disagrees. Applicant notes that the anemia of chronic disease should not be considered as a chronic inflammatory disease *per se*. Rather, the anemia is more properly considered as a possible accompanying symptom of the chronic disease.

Additionally, applicant points out that "anemia" is excluded from the phrase "symptoms associated with rheumatoid arthritis". Applicant has amended claim 14 accordingly.

Withdrawal of the obviousness rejection of claims 14-17, 21 and 22 is requested.

B. The method of treating symptoms associated with rheumatoid arthritis of claims 18, 19, 23 and 24 was rejected as obvious because the Office Action asserts that GB '304 teaches treating the anemia in rheumatoid arthritis patients by administering EPO for up to one week and because the Examiner asserted that it would be obvious to adjust the duration of EPO administration by observing the condition of the patients. Applicant respectfully traverse.

Applicant submits that one of ordinary skill in the art would not have been motivated to extend the duration of EPO administration in the method of GB '304 to treat anemia in rheumatoid arthritis patients because, in adjusting the EPO administration duration in rheumatoid arthritis patients, the artisan would find out that administering EPO for more than 2 weeks would not cause any statistically significant improvement in the anemia as shown in Table II of the instant specication. Therefore, the artisan would not have been motivated to administer EPO for at least 3 or 6 weeks in order to treat the anemia in rheumatoid arthritis patients as in the instant claims. Thus, there would have been no reason to extend the EPO treatment duration of GB '304 to at least 3 or 6 weeks required in the instant claims.

Applicant notes that GB '304 does not teach a method of treating the morning stiffness, painful and swollen joints, pain or a loss of grip strength in rheumatoid arthritis patients. Applicant has amended claim 18 and added claim

30 by limiting the symptoms treated to only the morning stiffness, painful joints, swollen joints, pain or a loss of grip strength. There would have been no suggestion or motivation based on GB '304 to treat morning stiffness, painful and swollen joints, pain or a loss of grip strength in rheumatoid arthritis patients.

Withdrawal of the obviousness rejection is requested.

Additionally, without admitting the claims 18, 19, 22, 24 and 30 were prima facie obvious over GB '304, applicant notes that Tables IV and V show that, unexpectedly, EPO treatments of at least 3 or 6 weeks were effective in treating morning stiffness, painful joints, swollen joints, pain or a loss of grip strength in rheumatoid arthritis patients. The unexpected results should overcome prima facie obviousness, if any, of claims 18, 19, 22, 24 and 30.

C. The method of ameliorating the disease activity of rheumatoid arthritis of claims 20, 25 and 26 was rejected as obvious because the anemia treated in the method of GB '304 was considered by the Examiner as a disease activity of rheumatoid arthritis and because the Examiner asserted that it would have been obvious to adjust the duration of EPO administration in the method of GB '304. Applicant respectfully traverses the rejection.

Applicant notes that anemia is excluded from the scope of the "disease activity of rheumatoid arthritis". Applicant has increased the duration of EPO

treatment to at least 3 weeks in claims 20, 25 and 26. Applicant submits that claims 20, 25 and 26 would not have been prima facie obvious over GB '304 because one of ordinary skill in the art would not have been motivated to extend the duration of EPO administration to treat anemia in rheumatoid arthritis patients because giving EPO for more than 3 weeks did not provide any statistically significant improvement on the anemia as shown in Table II of the instant specificatio. Even if, for argument purpose, that claims 20, 25 and 26 were prima facie obvious over GB '304, Table III shows unexpected results of reducing erythrocyte sedimentation rate and C-reactive protein levels in rheumatoid arthritis patients achieved by administering EPO for at least 3 weeks.

Withdrawal of the obviousness rejection of claims 20, 25 and 26 is requested.

Conclusion

With the above amendment and reasoning, applicants submit that the application is in a condition for allowance.

In case this paper is not timely filed, the undersigned hereby petitions for an appropriate extension of time. In the event that any fees are due in connection with this paper, please charge our Deposit Account No. 01-2300.

Respectfully submitted,
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